

Remarks

Obviousness Rejections

In paragraphs 4 and 5, the Office rejects claims 15-16, 23-24 and 30-37 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,534,546 to Honda et al.

The Office alleges that Honda et al. teach structurally similar compounds and compositions. In particular, the Office refers to claim 1 in column 262, when R_1 is NH_2 , m and n are 0, R_2 to R_4 are H. The Office also refers to the structure in column 31, lines 55-60 (example 36).

Applicants have amended claim 15 to specify that the substituents $-CH_2X^1$ and $-NHC(NH)NH_2$ of the claimed compounds of formula 1 are arranged in a para position to each other. Applicants respectfully submit that the claimed compounds having the specified substituents in the para-position have unexpected results compared to corresponding compounds having those substituents in the meta-position.

The K_i values for uPA of two meta-substituted compounds that, apart from their being meta-substituted instead of para-substituted, correspond to the compounds disclosed in the application as ST242 and ST293 (see Table 1), were tested. The K_i values of these meta-substituted compounds exceeded 1000, that is, the compounds tested negative for having inhibitory action on uPA. In contrast, as shown in Table 1 of the specification, para-substituted compounds ST242 and ST293 had K_i values for uPA of 36 and 2.4, respectively (Table 1, page 16, last listed compound and, page 17, second listed compound).

Applicants submit that these findings demonstrate that the para-substitution of

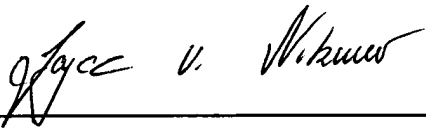
the currently claimed compounds confer unexpected results to the present invention, namely, inhibitory action with respect to uPA.

Upon request by the Office, Applicants will be pleased to submit the above data in form of a declaration.

Applicants also note that Honda et al. relates to a different technical field, namely NO synthase inhibitors, while the rejected pharmaceutical compositions have been disclosed in the specification as being useful as urokinase plasminogen activators.

As noted in the response submitted on October 31, 2003, Applicants respectfully submit that the Honda reference was cited for the first time in the final Office Action of July 31, 2003. Applicants also note that in response to the Office Action of March 25, 2003, Applicants had made some changes that were solely designed to bring the pending use claims into a format acceptable under U.S. standards. Applicants respectfully submit that the claim amendments made could have been reasonably expected. The claims were amended to pharmaceutical composition, compound and method of treatment claims. The claims rejected under 35 U.S.C. §103(a) are pharmaceutical composition claims comprising compounds substantially identical to those presented in the previously submitted use claims. Applicants also note that the Office appears to have treated the "use claims" that were pending at the time the Office Action of March 25, 2003 issued as compound claims as reflected in the rejection under 35 U.S.C. §102(b) made in this Office Action. In the present Office Action, the Office alleges that "Honda et al. teach structurally similar **compounds** and compositions as claimed herein." Accordingly, Applicants respectfully submit that the rejection over Honda could have been made in the Office Action of March 25, 2003. Thus, in order to allow for the development of clear issues between Applicants and the Examiner (MPEP §706.07), Applicants respectfully request that the finality of the Office Action be withdrawn.

In the event that this paper is not accompanied by the full fee required for its consideration, the Commissioner is authorized to charge any insufficient or missing fees to RFEM's deposit account No. 02-2135. The Commissioner is also authorized to deposit any overpayment to the same account. A duplicate copy for the financial branch is enclosed.

RESPECTFULLY SUBMITTED,			
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